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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,111	10/12/2006	Stefan Barth	3581. 10US01	1350

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EXAMINER	
MEAH, MOHAMMAD Y	
ART UNIT	PAPER NUMBER
1652	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/586,111	BARTH ET AL.
	Examiner	Art Unit
	MD. YOUNUS MEAH	1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,10,11,13,14 and 21-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 3, 4-5, 10-11, 13-14, and 21-26* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☒ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 4-5, 10-11, 13-15, and 21-26 are pending. In response to a previous non-final action mailed on 12/22/2010, Applicants on 06/22/2011 amended claims 1, 3, cancelled claims 2, 6-9, 12, 16-19 and 29.

Applicants' arguments filed on 06/22/2011 have been fully considered but they are found unpersuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections, 35 U.S.C 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 4-5, 10-11, 13-14, and 21-26 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claim 1 is drawn to a complex formed from component A and component B, wherein component A has binding activity for cellular surface structures and comprise any antibody derivatives or synthetic peptides having any structure. Moreover, claim 13 further limits the complex of claim 1 to encompass one or more supplementary

components S in addition components A and B. Thus, the claims encompass a genus of complexes comprising components A and S having essentially any structure and function. It is noted that derivatives of the recited components can encompass any compound which share any structural feature or any functional feature with the recited component. As such, derivatives are compounds having essentially any structure and/or function. Also, note that the genus of complexes claimed encompass (i) proteins having any structure which comprise a binding domain for any type of extracellular surface structure.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099- 1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 11) that complex of the present invention include, but are not limited to, a complex formed from at least one component A and at least one component B, wherein component A has binding activity for cellular surface structures, and component B carries a kinase as an effector function. Thus, while the specification reasonably conveys antibodies as component A, Dap-kinase as

component B, and a few specific examples of component S, there is insufficient written description of the infinite number of components encompassed by the genus of complexes recited because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics are not set forth in the specification as-filed. Therefore, the specification does not appear to be commensurate in full scope with the claimed invention. Vas- Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.

Claims 1, 3, 4-5, 10-11, 13-14, and 21-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an fusion protein comprising SEQ ID NO: 2 or 4 (see specification page 13), does not reasonably provide enablement for any immunokinase complex formed from component A and component B comprising DAP kinase, wherein component A comprise any molecule having binding activity for cellular surface structures or any antibody or derivatives or fragments thereof and wherein the complex further comprises one or more supplementary components S having any structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 3, 4-5, 10-11, 13-14, and 21-26 encompass a genus of complexes comprising components having component A having any structure and function. It is noted that derivatives of the recited components can encompass any compound which

share any structural feature or any functional feature with the recited component. As such, derivatives are compounds having essentially any structure and/or function. Also, note that the genus of complexes claimed encompass (i) proteins having any structure which comprise a binding domain for any type of extracellular surface structure. Thus, the claims encompass a genus of complexes comprising components having essentially any structure and function.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only few fusion proteins of specific amino acid sequences (SEQ ID NO: 2 and 4).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any fusion protein of any antibody molecule or fragments or modified fragments thereof or derivatives thereof with any kinase protein or derivatives thereof because the specification does **not** establish: (A) regions of the protein structure which may be modified the binding domain for any type of extracellular surface structure activity; (B) the general tolerance of binding activity of any protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues of a protein binding domain with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly include any complex comprising DAP kinase conjugated with any extracellular binding molecules or any antibody or derivatives or fragment thereof . The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of binding activity of any proteins binding domain, having the desired biological characteristics is unpredictable and the experimentation left to those

skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Argument

Applicants argument is considered and found partially persuasive as now amended claims comprise a fusion protein wherein DAP kinase having defined structure and function is conjugated to any binding domain having any structure and function. However claims still comprise the conjugate molecule comprising a binding domain comprising any antibody derivatives or synthetic peptides having any structure and function. Therefore as explained above the claims lack written description and enablement.

Claim Rejection - 35 U.S.C 102

Rejection of claims 1-7, 10-11, 13-14, 21, 25, 26 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Lavie et al (US 7419811, claim priority on US provisional 60/451207, 25 February 2003) and Lavie et al (WO 2004/078215, claim priority on US provisional 60/451207, 25 February 2003 from IDS) is withdrawn after amendment of the claims and applicants argument make the rejection moot. However Lavie et al is used for a 35 USC 103 rejection as explained below: This rejection is necessitated by applicants' amendment of claim 1.

CLAIM Rejection - 35 U.S.C 103 (a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a)A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4-5, 10-11, 13-14, and 21-26 are rejected under 35 U.S.C. 103(a) by Lavie et al (US 7419811, claim priority on US provisional 60/451207, 25 February 2003) and Lavie et al (WO 2004/078215, claim priority on US provisional 60/451207, 25 February 2003 from IDS) in view of Shohat et al (Biochem. and Biophy. acta 2002, 1600, pp 45-50).

Lavie et al teach fusion protein comprising DCK kinase conjugated to antibody which bind cell surface antigen (page 5). Lavie et al teach that the fusion complex further comprises an agent like a His tag to facilitate purification of the fusion protein (column 26, lines 34-50, reads on claim 13). Lavie et al also teach that said antibody of the conjugates bind to CD antigen (CD33, column 6 lines 41-60, reads on claim 26). However Lavie et do not teach said conjugate comprise a kinase moiety comprising DAP kinase. Lavie et teach the importance of conjugating a kinase enzyme molecule to an antibody that bind to cell surface antigen on the tumor cell for targeted delivery of the kinase enzyme to the tumor cell.

Shohat et al teach DAP-kinase family of molecule and teach that DAP kinase , a Ser/Trh kinase which is an important biologically important kinase and widely taught and used for programed cell death and important biomolecule for the treatment of cancer and other tumor related diseases.

Therefore, one knowledgeable in prior art is **motivated** to make the protein conjugate of Lavie et al comprising antibody that bind to tumor cell with DAP kinase as taught by Shohat et al. to cause programmed cell death of the tumor cells. One of skilled in the art find it obvious to make an antibody conjugate of DAP-kinase because such a conjugate will facilitate targeted delivery of the DAP-kinase kinase enzyme to the targeted tumor cells to which the antibody would bind and kill the tumor cells.

As such it would have been obvious to one of ordinary skill in the art to make the fusion protein of Lavie et al. using DAPk kinase as a kinase conjugating it to an antibody molecule and use the resulting conjugate to cause programmed death of the tumor cell.

Conclusion

Claims 1, 3, 4-5, 10-11, 13-14, and 21-26 are rejected and claim 15 is objected for depending on rejected claim. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah
Patent Examiner, Art Unit 1652

/Tekchand Saidha/
Primary Examiner, Art Unit 1652
8/26/11